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10/054,490

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Walter Prikoszovich

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EXAMINER

FISHER, ABIGAIL L

ART UNIT

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1616

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/054,490 | Applicant(s) PRIKOSZOVICH, WALTER | |
| | Examiner ABIGAIL FISHER | Art Unit 1616 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 56-58, 60, 64, 66-68 and 74-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 56-58, 60, 64, 66-68 and 74-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The examiner for your application in the USPTO has changed. Examiner Abigail Fisher can be reached at 571-270-3502.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 28 2008 has been entered.

Receipt of Amendments/Remarks filed on May 28 2008 is acknowledged. Claims 1-55, 59, 61-63, 65 and 69-73 were/stand cancelled. Claim 83 was added. Claims 56-58, 60, 64, 66-68, 74-83 are pending.

Abstract

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

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Where applicable, the abstract should include the following:

- (1) if a machine or apparatus, its organization and operation;
- (2) if an article, its method of making;
- (3) if a chemical compound, its identity and use;
- (4) if a mixture, its ingredients;
- (5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because the abstract refers to a specific NPL document without disclosing the steps taught in that NPL document which are required for the instant invention. The abstract must indicate the requirements that are to be met for the purified polymer if Applicant wishes to include this information in the abstract. Correction is required. See MPEP § 608.01(b).

Specification

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The specification is objected to for incorporating by reference essential subject material. Specifically, incorporated by reference is the requirement of the color strengths of reference solutions of B₂-B₉ of the brown color test. This test is specifically claimed however, the specification provides no guidance or support for the actual steps of the test.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-58, 60, 64, 66-68, 74-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: requirements of color strengths test. A claim must be able to stand on its own. Incorporation by reference is not permitted in claims. **Note: MPEP 2173.05(s)**. Since a claim must be able to stand on its own, the resulting claim is indefinite because the requirements of the brown color test are not set forth in the claim.

The term "purified state" in claim 72 is a relative term which renders the claim indefinite. The term "purified state" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The instant specification indicates that the polylactide meets two requirements, a metal ionic concentration of at most 10 ppm and color strengths of the reference solutions B₂-B₉ of the brown color test of the European Pharmacopeia. However, these requirements do not indicate the actual degree of purity. It is unclear, other than less than 10 ppm of a metal cation, how much impurity would meet the instant limitation of a purified state.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 56-58, 60, 64, 66-68 and 74-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bodmer et al (US Patent No. 5,538,739, cited in the Office action mailed on 11/28/07) in view of Brich et al. (GB 2,145,422, cited in the Office action mailed on 11/28/07) and Reiners et al (US Patent No. 4,879,402, cited in the Office action mailed on 11/28/07) or Bendix et al. (US Patent No. 4,810,775, cited on PTO Form 1449) and in further view of Eliot et al. (A Manual of Inorganic Chemistry, 1876) and as evidenced by Sigworth et al. (Journal of the American Water Works Association, 1972).

Applicant Claims

Applicant claims a pharmaceutical composition comprising a polylactide polymer in a purified state wherein the polylactide polymer in a purified state is an ester of a polyol containing at least three hydroxy groups and is off-white to white in color and wherein the polylactide in a purified state contains one or more metals in cationic form wherein the one or more metals have a concentration up to 10 ppm and a hydrophilic or lipophilic drug.

**Determination of the Scope and Content of the Prior Art
(MPEP §2141.01)**

Bodmer et al. teach sustained release formulations of drugs, particularly somatostatin or octreotide, in a biodegradable and biocompatible polymer carrier (column 1, lines 13-19). The preferred polymers are linear polyesters. Linear polylactide-co-glycolides which have a molecular weight between 25,000 and 100,000 and a polydispersability between 1.2 and 2 are taught (column 8, lines 1-4). One preferred polymatrix is poly(lactide-co-glycolide)glucose (abstract and examples). It is taught that sustained release formulations can be in the form of a implant or microparticle (column 12, lines 20-25). The molar ratio of lactide:glycolide is from about 75:25 to 25:75 including 60:40 to 40:60 (column 9, lines 18-20). Star polymers having a molecular weight from 10,000 to 200,000 and a polydispersity from 1.7 to 3.0 are taught (column 8, lines 35-40). It is taught that the polyester are known and described in GB 2145422 to Brich et al. (column 8, lines 7-8 and example 4).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

Bodmer et al. do not teach the synthesis of the polyol esters and subsequently the purification of the polyol esters. However, this deficiency is cured by Birch et al. and Reiners et al. or Bendix et al.

Birch et al. teach the preferred synthesis of the polyol esters taught in Bodmer et al. It is taught that the ester is formed in the presence of a catalyst which makes ring

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opening and polymerization feasible. The preferred catalyst is Sn-octoate (page 2, lines 37-41). It is taught that the formed polyol ester produced may be purified and isolated in a conventional manner (page 2, line 47).

Reiners et al. teach synthesis of (meth)acrylic acid derivatives containing urethane prepared by reaction of a (meth)acrylic acid ester with diisocyanates and subsequent reaction with polyols (abstract). Example 5 teaches polymer formation utilized tin octoate. After the solvent is removed (after filtration over active charcoal) a colorless highly viscous liquid is produced.

Bendix et al. is directed to a process for purifying resorbable polyesters. It is taught that if it seems necessary, the actual precipitation may be preceded by additional purification stages such as filtering with the addition of activated charcoal. The polyester can then be precipitated from the polymer solution in the presence of a precipitation agent (column 4, lines 5-13). Exemplified polyesters include poly(lactide-co-glycolide).

Bodmer et al. do not teach the respective color of the resulting polymer. However, this deficiency is cured by Reiners et al. Eliot et al.

Reiners et al. teach in Example 5 teaches polymer formation utilized tin octoate. After the solvent is removed (after filtration over active charcoal) a colorless highly viscous liquid is produced.

Eliot et al. teach that charcoal is known not only to destroy odors but it removes colors as well. For this color removing purpose it has long been employed in the purification of sugar and of many chemical and pharmaceutical preparations. It is

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taught that almost any coloring matter can be removed from a solution by filtering the liquid through a layer of charcoal (page 308, 388.). It is also taught that charcoal can also absorb many other substances besides coloring matters such as sulphates and metals like gold or silver (page 309, first paragraph).

***Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Bodmer et al., Birch et al., and Reiners et al. or Bendix et al. and utilize activated charcoal in the purification of an ester of a polyol. One of ordinary skill in the art would have been motivated to utilize activated charcoal as Birch et al. teach that the synthesis of the polymers of Bodmer et al. include utilizing tin octoate as a catalyst and then purifying and isolating in a conventional manner. Both Reiners et al. and Bendix et al. teach that in the purification of polymers it is known to utilize activated charcoal.

Regarding the claimed color, Eliot et al. teach that activated charcoal has been known for a long time to be utilized to remove unwanted colors in pharmaceutical preparations. Since Reiners et al. teach that filtration over active charcoal produces a colorless liquid, it is the examiner's position that utilizing activated charcoal in the purification of the polymers taught by Birch et al. would possess the same color as instantly claimed.

Regarding the claimed amount of metal ion present, the instant specification teaches that precipitation of the polylactide from an organic solvent contains about 2

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ppm of the metal cation (page 1). Since Reiners et al. teach this type of precipitation to purify the polyesters, there is a reasonable expectation that it would possess about 2 ppm of the metal cation. However, additionally if activated charcoal is additionally utilized in the purification process, one of ordinary skill in the art would expect even less metal cation. As evidenced by Sigworth et al., tin is the most readily adsorbed metal of any studied on activated carbon (page 33, left column, last paragraph).

Response to Arguments and Declaration under 37 SCR 1.132

Applicants argue that (1) one of ordinary skill in the art would not recognize that activated charcoal will bind the octoate chain, removing the tin counter ion as well. Applicants argue that in practice the activated charcoal will remove the tin metal ion but a second purification step is required to remove the ethyl hexanoate acidic group which remains. Therefore even if one of ordinary skill in the art were to combine the Reiners with Bodmer and GB-422 at least the ethyl hexanoate impurity would remain. Applicants have submitted a technical report from Ciba wherein the polymer was investigated after charcoal treatment and all of the fractions had ethyl-2-hexanoate present but had lowered tin content.

Applicants' arguments filed May 28 2008 have been fully considered but they are not persuasive.

Regarding applicants arguments, the examiner acknowledges the Ciba report in which the polymers after charcoal treatment had ethyl-2-hexanoate present, however, the instant claims do not exclude ethyl-2-hexanoate from being present. The requirements

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of the instant claims are that there be at most 10 ppm of a metal and that the color is white to off-white. As indicated above, activated charcoal is known in the art to not only be utilized to purify pharmaceutical preparations to remove color but tin is also known to be one of the most readily adsorbed metals on activated charcoal. Therefore, applicants' argument that it is surprising that activated charcoal can remove tin is not really that surprising. Since it would have been obvious to one of ordinary skill in the art to utilize activated charcoal in the purification of the esters of polyol, the amount of tin present would be in an amount instantly claimed. It is noted that the features upon which applicant relies (i.e., removal of ethyl-2-hexanoate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Mr. Schneider argues in the Declaration that (1) he is of the opinion that one of ordinary skill in the art would not combine the Bodmer, GB '422 and Reiners reference as the chemistry involved in the Reiners reference is completely different from that of Bodmer and GB '422. Reiners is directed to acrylic acid derivatives containing a urethane groups whereas Bodmer and GB '22 describe the formation of polyesters. Mr. Schneider argues that (2) Reiners generally operates in the field of dental polymer which is different than the field of the present invention, namely pharmaceutical formulation. Therefore, he is of the opinion that one would not look to a reference such as Reiners when attempting to purify a pharmaceutical polymer. Mr. Schneider argues

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that (3) Reiner does not teach removal of tin octoate catalyst from a polymer by activated charcoal treatment. Mr. Schneider argues that (4) at least the ethyl hexanoate impurity would remain in the polymer.

The declaration under 37 CFR 1.132 filed September 7 2007 is insufficient to overcome the rejection.

It is noted that the Rule 132 Declaration is an opinion Declaration and has been given little weight since it does not provide any factual evidence.

Regarding the first argument, Reiners et al. describes the synthesis of polymers utilizing tin octonate. One of ordinary skill in the art would have been motivated to look at Reiners as an alternative to removal of the tin octonate as it is directed to formation of polymers utilizing the same catalyst. The fact that the polymers are different (i.e. polylactide vs. polyacrylates) would not persuade one of ordinary skill in the art against utilizing active charcoal in the purification. Furthermore, if even the argument were persuasive it was known in the art to utilize activated charcoal to purify polyesters as Bendix et. al teach utilizing activated charcoal to purify polyesters.

Regarding the second argument, a reference in a field different from that of applicant's endeavor may be reasonably pertinent if it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his or her invention as a whole. **Note:** MPEP 2141.01 (a) [R-6]. In the instant case both Reiners et al. and Birch et al. teach formation of polymers utilizing tin octoate. Reiners et al. teach a purification method of the polymer which is quite simple only involving filtration over activate charcoal and solvent removal. One of

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ordinary skill in the art would have been motivated to look at Reiners et al. when desiring a method of purifying a polymer after the addition of a catalyst such as tin octoate.

Regarding the third and fourth arguments, the rejected claims do not require that there is no ethyl hexanoate present therefore, those arguments are not persuasive in overcoming the art rejections of record. The only requirement of the claims is that there is less than 10 ppm of metal cation and that it is white to off-white in color. As indicated above, activated charcoal was known to remove tin and remove coloring material, therefore, there is a reasonable expectation that purification of the esters of polyol utilizing activated charcoal is white to off-white and contains little if any tin.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Claim 83 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bendix et al. in view of Sigworth et al.

Applicant Claims

Applicants claim a method of removing tin from a polylactide polymer comprising the step of contacting a polylactide polymer with activated charcoal.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

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Bendix et al. is directed to a process for purifying resorbable polyesters. Exemplified polyesters are poly(lactide-co-glycolide). It is taught that if it seems necessary the actual precipitation may be preceded by additional purification stages such as filtering with the addition of activated charcoal. The polyester can then be precipitated from the polymer solution in the presence of a precipitation agent (column 4, lines 5-13). Example is directed to the purification of a poly(DL-lactide) utilizing only the precipitation technique wherein 138 ppm of the Sn catalyst was used in the reaction and 34 ppm remained after precipitation.

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

Bendix et al. do not exemplify utilizing activated charcoal in the purification. However, Bendix et al. do teach that the actual precipitation may be preceded by purification by filtering with the addition of activated charcoal. Bendix et al. do explicitly state that the activated charcoal will remove the tin. However, this deficiency is cured by Sigworth et al.

Sigworth et al. is directed to the adsorption of inorganic compound by activated carbon. It is taught that tin is the most readily adsorbed metal of any studied on activated carbon (page 33, left column, last paragraph).

**Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)**

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It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize activated charcoal in the purification of polylactide polymers. One of ordinary skill in the art would have been motivated to utilize activated charcoal as Bendix et al. teach that precipitation purification may be preceded by filtration with addition of activated charcoal. Therefore, one of ordinary skill in the art would have been motivated to additionally utilize activated charcoal in order to further purify the polymer as taught by Bendix et al.

Regarding the claimed removal of tin, since it was known at the time of the instant invention that tin is one of the most readily adsorbed metals, the purification step taught by Bendix et al. which includes filtration using activated charcoal would necessarily remove the tin. Furthermore, one of ordinary skill in the art would have been motivated to add activated charcoal if a tin catalyst is utilized since it was known that tin is readily adsorbed on the activated carbon.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

/Mina Haghighatian/
Primary Examiner, Art Unit 1616